OPTN Pediatric Transplantation Committee
Meeting Summary
May 18, 2022
Conference Call

Evelyn Hsu, MD, Chair
Emily Perito, MD, Vice Chair

Introduction

The OPTN Pediatric Transplantation Committee (the Committee) met via Citrix GoToMeeting teleconference on 5/18/2022 to discuss the following agenda items:

1. Policy Oversight Committee (POC) Update
2. Validating Estimated Post-Transplant Survival Scores (EPTS) for Pediatric Candidates Data Request
3. Project Updates

The following is a summary of the Committee's discussions.

1. Policy Oversight Committee (POC) Update

The Vice Chair presented an update from the Policy Oversight Committee (POC).

Presentation Summary:

The POC is currently working to define project benefit and develop a method to rate various attributes. Some attributes discussed have been number of patients affected, level of impact to those patients, and vulnerable populations affected. The goal is to create a more objective measure to evaluate a project's potential impact to the community and considering its sequencing and prioritization. The POC's ultimate goal is to maximize benefit given the available resources.

As part of the prioritization and sequencing that the POC does, one consideration is how much capacity each committee has to take on more work, but also how much capacity the OPTN staff have to actually implement the planned changes. This capacity, in terms of staff hours, has been fairly constant for quite a while, and the POC has identified a need to increase this capacity. More of the projects involve significant resources to implement, and the work remains important to the community. The POC is currently working with the Finance Committee to request an increase in the available resources for implementing committee work in the next OPTN budget cycle. Capacity, budget, prioritization, and sequencing considerations will result in a shift in committee work:

- More discussions about scope earlier on in projects
- Information technology (IT) Staff more actively involved in discussing potential options for system solutions earlier in projects
- Some projects may not move as quickly until implementation capacity can be increased

Summary of discussion:

The Chair stated that when they were on POC it was a nice way to see where the Committee fit in the policy development process. There Chair mentioned that they had felt outnumbered on the POC and suggested that there were challenges to advocating for pediatrics in that setting.

The Vice Chair stated that they hope standardizing project benefits will help some, but also noted that projects with a large impact on pediatrics may not actually be about pediatric allocation.

The Chair also mentioned that the POC is a nice way to get wind of projects that might impact pediatric patients so it can be brought back to the Committee. The Chair emphasized how important it is to be versatile when on the POC since pediatric advocacy spans across all organ types.

The Vice Chair noted that there has been an increased recognition of, not just pediatrics, but vulnerable populations in general.

The Vice Chair and Chair emphasized the importance of communication, speaking up/asking questions, and building relationships, especially with members that don't have pediatric expertise.

There was no further discussion.

2. Validating Estimated Post-Transplant Survival Scores (EPTS) for Pediatric Candidates Data Request

Staff presented an overview of the Validating EPTS for Pediatric Candidates data request, and the Committee voted to approve the data request.

Presentation summary:

The goal of this data request is to evaluate the predictive ability of estimated post-transplant survival scores (EPTS) in pediatric patients. EPTS will be used in Kidney and Pancreas Continuous Distribution to model post-transplant survival. If EPTS is not accurately predictive of survival in pediatric patients, an alternate solution, such as assigning all pediatric patients the same low EPTS score. The data request has two foci, to evaluate the predictive ability of EPTS in pediatric patients, and if predictive, evaluate predictive ability within sub-populations.

Evaluating Predictive Ability

- Consider 10-year post-transplant survival
- Calculate EPTS for a pediatric cohort using the adult EPTS formula
- Create a Cox model to model survival as a function of the EPTS calculated on pediatric patients
- Calculate the c statistic for this model and potentially compare it to literature on the predictive ability of EPTS in adult recipients as applicable

Equity considerations are important to ensuring organs are allocated fairly. Fairness can be defined in a variety of ways, including equity in access and utility, which is what EPTS intends to measure. The Kidney and Pancreas Continuous Distribution Workgroup gave EPTS a weight of 5 percent for their first round of modeling, which means EPTS will make up 5 percent of a candidate's composite allocation score. The CAS utilizes EPTS to capture survival probability alone, and accounts for equity in other factors.

If EPTS is found to be predictive of pediatric post-transplant survival, a secondary data request may be necessary to ensure that pediatric sub-populations are not disadvantaged relative to other pediatric patients because EPTS is less predictive within that sub-population.

Summary of discussion:

The Vice Chair inquired why this is coming up now and why EPTS isn't already being calculated for pediatrics. A member explained that when the new kidney allocation system was implemented in 2014, this scoring system was generated to help with longevity matching. In the current system, adults with an EPTS less than 20 get priority for good quality low kidney donor profile index (KDPI) kidneys and, right now, that's the only way EPTS is used. The member continued by explaining that, with the move to continuous distribution (CD), there is a focus on longevity matching, which means that the EPTS score

will be used much more broadly. The member stated that the EPTS score was generated using data across the full range of transplant candidate ages. However, there wasn't data that separated out how well EPTS actually performed amongst kids, which was concerning because it's not highly predictive for adults. The member noted that the c statistic across all patients is only 0.69, which isn't very high.

The member explained that there are four factors that go into the EPTS score: (1) candidate's age (younger being the lower score), (2) how long the candidate has been on dialysis (higher score for more time on dialysis), (3) diabetes, and (4) previous transplant. The member emphasized that, when thinking about pediatric patient survival, these are not the factors that they would immediately consider as being highly predictive.

The member mentioned that they reviewed data on the current pediatric waitlist and about 70 percent of pediatric patients would have the lowest EPTS score of 1 using this adult focused score and about 90 percent would have an EPTS less than 5. The member noted that the concern is that the EPTS score would actually compare pediatric candidates against each other on the match run in CD and there is no evidence demonstrating that that is appropriate. The member concluded that that is how these discussions started and mentioned that, their personal hypothesis, is that EPTS is not very predictive so it probably shouldn't be calculated for pediatrics in CD.

The Vice Chair appreciated the context provided and thought it was interesting that longevity matching, or how long a patient will survive post-transplant, exists in kidney allocation but doesn't in other organ allocation systems. The Vice Chair mentioned that it's a concept that could possibly be incorporated into CD for every organ, so it's important to think about how to execute it.

A member noted that, in some ways, this concept exists in a very limited area of liver matching, i.e., young recipients are prioritized for livers from younger donors.

The Chair inquired about the intention of sharing the results of this data request – is there a consideration for presenting the results at national meetings or writing a manuscript? The Chair also inquired if any Committee members are interested in contributing to those efforts. Staff mentioned that they are not able to take the lead on writing a manuscript, but can help with facilitating the Health Resources and Services Administration (HRSA) process if a member wants to write it. Staff also noted that they can help format graphics and provide a supporting role. Members volunteered to help with this effort.

A member agreed that the results of this data request should be made publicly available; however, the proceedings of the Committee are not as easily searchable online as a published manuscript on PubMed. The member highlighted that, especially if the Committee advocates for all pediatric candidates to be assigned the lowest possible EPTS score, it's also going to be important for the logic behind these results to be available for anyone to access.

A member also explained, for those who may be concerned with the weights for pediatric priority (15 percent) and EPTS (5 percent), those weights are preliminary weights used for the first round of modeling. The member noted that there were a couple more extreme versions of the model with different weights for the different attributes, and those modeling results will be presented to the Kidney and Pancreas Continuous Distribution Workgroup in August so adjustments can be made as needed.

The Chair thanked those members that volunteered to help work on a manuscript for submission and emphasized that this is such a great venue for being an advocate for kids but also for building on academic growth.

A member stated that the request is looking at 10 years' worth of data and then 10 year survival. The member inquired how far back in time will this data go and if staff is planning on subdividing pediatric

patients by age groups. Staff explained that they are planning on using all pediatric kidney transplants from 2001 to 2011, which most closely matches the methodology used to create the original EPTS score. Staff mentioned that a 10 year survival window should give them enough candidates to hopefully draw some conclusions. Staff also explained that stratifying pediatric candidates by age group would be part of the second data request, if warranted, which would look at different pediatric subpopulations such as age group and blood type.

A member inquired if there is any data on accurate EPTS is for adults. A member stated that, as mentioned before, there is the original white paper which gave a c statistic of 0.69. The member explained that there is available data on the accuracy of EPTS for adults, but no data for pediatrics. A member also noted that when they try to use the online EPTS calculator, it won't calculate a score for anyone under 18 years old.

A member mentioned that they were confused how EPTS would apply for pediatrics. The member stated that, since the data request is going back to 2001, it is looking at multiple eras where kids had different priority in order to get them transplanted, especially when centers were trying to get pediatric candidates transplanted within six months or one year depending on their age. The member continued by stating that the pediatric candidate's age would benefit them; however, transplant in kids with diabetes is almost unheard of unless it's a teenager and the pediatric candidate's time on dialysis is front loaded to be low. The member mentioned that that may be the point of this data request – to demonstrate that EPTS is inapplicable to pediatric candidates.

A member stated that all of those reasons were the arguments for why EPTS isn't currently used for pediatric candidates. The member noted that the fact that diabetes is rarely the cause of kidney failure in children probably works to their advantage because having diabetes results in a worse EPTS score. The member also mentioned that it's similar with time on dialysis – more time on dialysis results in a worse EPTS score. The member explained that these factors could benefit a pediatric candidate's EPTS score but there isn't data.

The Vice Chair mentioned that the Committee members with kidney expertise were asked to give guidance on how to use EPTS for pediatric candidates in the CD framework. The two options for incorporating pediatrics into EPTS were to either assign all pediatric candidates the lowest possible EPTS score, which 70 percent of kids get anyway, or to calculate an EPTS score for them. The Vice Chair explained that those members came to the conclusion that pediatric candidates should either be given the lowest score or data should be used to try to come to an evidence based answer.

A member mentioned that they were worried about the infants who start dialysis as babies. Generally, kidneys are not transplanted into kids with birth problems related to kidney disease who are less than 10 kilograms (kg), which is about 18 months to two years old. The member explained that an infant who started dialysis at two months old and had been growing on dialysis for 2 years is going to be ranked below a patient who maybe had some kidney disease but didn't need to start dialysis. The member emphasized that that's unfair to disadvantage those babies in the system.

Staff inquired if there was any opposition to the Committee submitting this data request. The Committee unanimously supported the data request.

3. Project Updates

The Committee reviewed the status of their current projects and collaborations, including the OPTN Heart Transplantation Committee's Pediatric Heart Blood Type Incompatible (ABOi) project, the OPTN Kidney and Pancreas Committees' Continuous Distribution project, and the OPTN Liver and Intestinal Transplantation Committee's Continuous Distribution and National Liver Review Board (NLRB) projects.

Pediatric Heart ABOi Workgroup Update:

The Pediatric Heart ABOi Workgroup met on 05/10/2022 to further review policy modifications.

The Pediatric Heart ABOi Workgroup discussed proposed "slotting" of the tertiary blood type match rows in current heart allocation, as in OPTN Policy's *Table 6-7: Allocation of Hearts form Deceased Donors at Least 18 Years Old*, and the factors considered in determining where to slot those groups.

- Consensus reached that slotting the tertiary groups in the adult deceased donor match run order should be done in a way that maintains the existing priority of adult statuses, wherever possible

The Pediatric Heart ABOi Workgroup also considered potential data collection and data reporting opportunities

- Most recent titer info, graft failure, and death information is already collected by the OPTN
- Discussed potentially adding a question to the Transplant Recipient Follow-up (TRF) form to identify whether the recipient was receiving AB reduction therapies. It was decided that staff would draft a memo to the Pediatric Heart Transplant Society (PHTS) request that they consider colleting certain data elements, include post-transplant AB reduction therapies. The Workgroup members would present the memo to PHTS.

Summary of discussion:

The Pediatric Committee representative on the Pediatric Heart ABOi Workgroup agreed this was an accurate update, and noted that the Pediatric Heart ABOi Workgroup hopes to finalize the proposal soon.

The Chair commented that, because different antibody therapies could affect patient outcomes, data would be collected to track the different therapies and guide future antibody therapy use, similar to current data collection on immunosuppression. The member agreed, and explained that this could open the door to performing ABOi transplantation in new scenarios. The member added that this is an opportunity to collect data around this that could enhance understanding of ABOi transplant, without overly burdening programs. The member shared that other members of the Pediatric Heart ABOi Workgroup had concerns regarding data burden, but that there will be questions about additional data collection when this proposal is released for public comment.

The Chair asked if the main metric used to monitor this policy change would be waitlist mortality, in terms of the availability of ABOi to certain age groups and patients. The member noted that it would be important to ensure that waitlist mortality has improved, but that it would also be critical to monitor the outcomes of recipients who receive ABOi transplants at a high titer. The member continued that the tire data under which these transplants occur matters, as does the titer levels over time. The member emphasized that this data should be collected.

Kidney-Pancreas Continuous Distribution Workgroup Update:

The Kidney and Pancreas Continuous Distribution Workgroup submitted their first modeling request to the Scientific Registry of Transplant Recipients to the SRTR at the end of April. The combined analytic hierarchy process (AHP) results has pediatric priority weighted at 15 percent for kidney, and 20 percent for pancreas and kidney-pancreas (KP). This Workgroup is currently discussing operational items, such as review board, national kidney offers, and facilitated pancreas, while awaiting modeling request. A second concept paper will be released in the Summer 2022 public comment cycle.

Summary of discussion:

The Chair asked if the 15 percent weight given in the first modeling request translated to 15 points out of 100 total points. A member confirmed this, and explained that each attribute has its own rating scale to determine score, with some attributes having a binary scale, like the pediatric attribute, and others having a more continuous scale, such as distance from donor hospital. If the candidate is pediatric, they would receive 15 total points for that attribute, while an adult candidate would receive no points. The member continued, explaining that weight of each attribute combined sums up to 100 percent. The member noted that 15 percent is a high weighting relative to the other attributes in the modeling request.

The Chair pointed out that the pediatric attribute was weighted higher in the lung continuous distribution framework, and wondered what the pediatric attribute would be weighted in liver continuous distribution. A member responded that the pediatric attribute was given a weight of 20 percent in the lung continuous distribution allocation framework. Staff confirmed this.

OPTN Liver and Intestinal Organ Transplantation Committee Project Updates

The OPTN Liver Committee has begun discussions to develop a continuous distribution framework for liver allocation. Including identifying attributes in current policy and additional attributes for considerations, categorizing attributes according to goal, and finalizing attributes to be included in further framework discussions.

- Pediatric priority is currently considered in liver allocation policy, and will continue to be included as part of the liver allocation system

The primary goal of continuous distribution is to eliminate hard boundaries built into the current classification based system, resulting in more equity for patients in addition to more transparency in the system. In the process of converting the current system to continuous distribution, the Liver Committee has the opportunity to include other attributes that don't exist in current policy. The Liver Committee is working to determine which attributes are most important to include in the first version of continuous distribution. To do this, a small group of Liver Committee members and subject matter experts will be assigned to research each attribute. Liver Committee members will lead discussion for each assigned attribute during upcoming meetings. The Liver Committee will decide if the attribute should continue to be considered for inclusion in the first iteration of CD.

- The Liver Committee must balance time, resources, community consensus, impact on other organ systems, the size of the impacted population, and the benefit for that impacted population
- The main goal is to identify attributes which can be easily incorporated that will have a significant impact on the identified goal

The OPTN Liver Committee is also continuing their ongoing review of NLRB diagnoses. Since implementation of the NLRB in 2019, the Liver Committee has routinely reviewed NLRB policy and guidance to ensure it remains updated and accurate. As part of the most recent review, the Liver Committee discussed cystic fibrosis exception policy, and received the following feedback from the Pediatric Committee:

- Current cystic fibrosis standard pediatric end stage liver disease (PELD) and model for end stage liver disease (MELD) exceptions are not relevant to pediatric liver transplant, and are more specific to lung-liver transplant. Pediatric cystic fibrosis liver disease is a different entity
- Pediatric liver transplant candidates with cystic fibrosis have severe liver disease, like other children with severe liver disease

The Liver Committee convened a group of pediatric subject matter experts to draft guidance for pediatric candidates with cystic fibrosis. The Liver Committee will review the proposed guidance, and vote to send this guidance to public comment in August.

Summary of discussion:

The Chair emphasized the importance of cross-committee communication, to ensure pediatric interests and perspectives are represented.

One member asked if any pediatric pulmonologists were involved in drafting the guidance for pediatric cystic fibrosis patients, and the Chair confirmed there was at least one pediatric pulmonologist.

There was no further discussion. The meeting was adjourned.

Upcoming Meetings.

- June 15, 2022 (Virtual)

Attendance

- **Committee Members**
  - Evelyn Hsu
  - Emily Perito
  - Abigail Martin
  - Brian Feingold
  - Caitlin Peterson
  - Caitlin Shearer
  - Dan Carratturo
  - Geoffrey Kurland
  - Jennifer Lau
  - Namrata Jain
  - Rachel Engen
  - Regy Gonzalez Peralta
  - Shellie Mason
  - Walter Andrews
  - Warren Zuckerman
  - William Dreyer
- **HRSA Representatives**
  - Jim Bowman
  - Marilyn Levi
  - Raelene Skerda
- **SRTR Staff**
  - Bryn Thompson
  - Jodi Smith
- **UNOS Staff**
  - Rebecca Brookman
  - Matt Cafarella
  - Amanda Robinson
  - Kaitlin Swanner
  - Kristin Cuff
  - Robert Hunter
  - Samantha Weiss